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The Adaptability of Individuals to Shiftwork. A Possible Experimental Approach.

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Introduction

The Institute for Occupational Physiology at the University of Dortmund has been an important research center for shiftwork. This line of research was terminated a decade ago, when Joseph Rutenfranz died in 1989 and Peter Knauth became Professor at the University of Karlsruhe. Now, this topic will be resumed by a scientist with an extended experience in sleep research focused on experimental studies and field observations on sleep disturbances as caused by environmental noise [10, 11]. Research on shiftwork now will be executed in close cooperation with the biochemical unit of the institute.

The project outlined here is still in the stage of planning, the first part will probably start within some weeks. It aims at the clarification of the individually determined ability to adapt to shiftwork and the question whether and by which tests this ability can be diagnosed during medical occupational check-ups. This is particularly relevant for those organisations, e.g. the army where the personnel operate with extremely expensive worktools and/or whose professional activities may impose a considerable hazard to others.

Shiftwork

At present, 15 – 20 % of the employees in the European Union are performing shiftwork. In many industrial sectors as well as in the army missions during the night are not only planned at long-term but also ordered at short-term. The immediate consequences of these shifts, from day- to nightshifts and the reverse, from night- to dayshifts are desynchronizations of physiological functions. These disturbances are – among others – characterized by impairments of sleep, of well-being, and performance. Additionally, spontaneous sleep periods are expected to occur in about one fifth of the employees during work [1] and thought to play a major role in many accidents [15, 22]. The full adaptation to the new time regimen needs one day on the average per hour of relative time shift. Repeated time shifts, i.e. repeated adaptations to nightshifts and readaptations to dayshifts evoke repeated stress for the whole organism and may accelerate the genesis and manifestation of nonspecific chronic diseases for persons with increased vulnerability in the long run [23].

Circadian rhythm

The circadian rhythm is controlled by the light-dark cycle and mediated by melatonin, the hormone that is produced in the pineal gland. It adopts the role of a pacemaker for the synchronization of physiological

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functions (core temperature, heart rate etc. [3, 4]).

The temporal course of the melatonin synthesis is closely related to the periodical alterations of body core temperature which was and is still usually registered in studies on the circadian rhythm and the effects of shiftwork. As the production of melatonin is directly controlled by the endogenous pacemaker the actual concentration of that hormone is a more reliable indicator of the individual circadian phase and of related disorders than rectal temperature, in particular, as the latter is more sensitive to masking effects due to different environmental influences. The major advantage of the registration of rectal temperatures is that this variable can be recorded continuously and at low costs.

Inhibition of the melatonin synthesis

The production of melatonin is not only inhibited by natural but also by artificial light; hereby wavelength, intensity and duration of light play an important role [5, 6, 13, 21, 25]. The direction of the light-induced phase shift depends also on the time of application. Light in the evening causes phase delays whereas light in the morning leads to phase advances [14]. It is therefore concluded that adaptation to nightwork can be facilitated by the application of light.

The success of those measures is, however, debated as shiftworkers are exposed to contradictory zeitgebers [12, 17]. Additionally, due to the interindividual extremely different phases (up to 10 hours, morning-, evening types), the effects of light that is applied at a defined time of the day must evoke different effects in different persons [7, 8, 18, 19, 20]. Moreover, in the real situation various other competing zeitgebers might influence the organism, e.g. other parts of the electromagnetic spectrum (UV-A radiation, low-frequency magnetic fields).

Adaptation to shiftwork

Several studies revealed that a certain percentage of individuals is not able to adapt to shiftwork. Some authors reported that particularly those persons with a late circadian phase (evening types) have only minor difficulties to cope with nightwork [16]; where other authors reported the same for persons with a smaller amplitude of their core temperature ('individuals with low amplitudes have less to invert and adapt more easily' [2, 24]). A clear allocation between person-related characteristics and the ability to adapt to shiftwork, is at present, however, not possible. Based on a few studies on this problem and on the strong correlation of body core temperature on the one hand and the amount and the course of melatonin synthesis on the other hand it is possible to derive the hypothesis that persons with late circadian phases (evening types) and small amplitudes of their body core temperature produce less melatonin and adapt better to shiftwork than persons with early circadian phases (morning types).

Hypothesis: A late circadian phase is associated with a low amplitude of rectal temperature and of melatonin production. Those persons adapt more easily to shiftwork than those with an early circadian phase, with high amplitudes of rectal temperature and of melatonin production.

An important aspect of the intended studies is therefore the question of an individual characteristic of melatonin production and a concomitant individual adaptability to shiftwork.

Outline of the project

The project will be executed in four steps, where the hypotheses, the procedure and the methods applied may deviate to those presented below according to the results of the preceding step(s):

[1] **Step 1 (pilot study)** aims at the determination of the relationship between subjective circadian phase and the amount of melatonin production during the night.

[2] **Step 2 (constant routines)** will be performed to examine the relationship between subjective circadian phase and the course and the amplitudes of rectal temperature and of melatonin production over a time period of 24 hours.

[3] **Step 3 (experimental shiftwork)** is planned to elucidate the role of individual characteristics for the adaptability to nightwork under strictly controlled conditions in the lab, i.e. to determine the resistance to adapt to nightwork even in case of facilitating measures.

[4] **Step 4 (prospective study)** aims to clarify whether an individual adaptability to nightshifts can be predicted on the basis of individual features.

Methods

Step 1 – Hypothesis: A late subjective circadian phase is associated with a late melatonin peak and a low melatonin production.

The **pilot study** shall elucidate the assumed relationship between the individual circadian phase, the course and the amount of melatonin production. The hypothesis is that the quantity of melatonin production is lower and the peak of melatonin production is later in persons with a self-rated late circadian phase (evening types) as compared to persons with an early phase (morning types).

About 100 patients of the surgical unit of a military hospital fill in a questionnaire which proved to be a valid instrument for the determination of the subjective circadian phase. The actual concentration of salivary melatonin of these persons will be determined hourly during one night (6 pm to 6 am) and the excretion of 6-hydroxymelatonin sulfate at 3 hour intervals. This time space is sufficient to determine reliably the maximum of melatonin synthesis during the night. Personality variables will be determined by suitable inventories (Freiburg Personality Inventory, FPI). A military hospital is chosen for that pilot study as the respective patients are relatively young and healthy. Those with internal diseases are excluded from participation.

Step 2 – Hypothesis: The course and the amplitude of body core temperature is closely related to the course and the peak of melatonin production (and with the self-rated circadian phase).

The **constant routines** consist of 24-hour-observations to determine the relation between the subjectively rated circadian phase, the course and the amplitude of rectal temperature and of melatonin production: Due to economical reasons these observations shall be designed as the basis for the prospective study outlined under step 4 and therefore performed with persons who regularly or occasionally work at night during their professional carrier. 100 to 200 persons fill in a questionnaire (the same as in the pilot study) to determine the subjective circadian phase and spend 24 hours (noon to noon) under constant conditions (< 50 lux). This procedure (constant routines) is according to an agreed opinion of several authors essential to determine the actual circadian phase with sufficient accuracy [25].

During the observation period the actual concentration of salivary melatonin will be measured hourly, the excretion of 6-hydroxymelatonin sulfate for every 3 hour-periods. Rectal temperatures, heart rates, and body movements shall be recorded continuously throughout. Personality variables will be determined with a suitable inventory (FPI).

The results of the pilot study and the constant routines determine the extent of the third and the fourth step.

Step 3 – Hypothesis: Individual features (self-rated circadian phase / course and amplitude of body core temperature or of melatonin production) determine the inability to adapt to shiftwork. This resistance is expected even in case of targeted facilitations.

Experimental shiftwork under strictly controlled conditions shall be performed as the effects expected here might be considerably masked due to a vast number of environmental influences that are unavoidable in the real situation at the workplace.

Exposure to light suppresses the synthesis of melatonin and has been shown to facilitate the process of adaptation to nightwork. If the suppression of melatonin synthesis is – as reported by Graham et al. [9] – greater in persons with habitually low melatonin levels, these persons are expected to be even more resistant against adaptation in case of targeted exposure to bright light.

After the individual circadian phase is determined using a constant routine persons with early and with late circadian phases (habitually high and low levels of melatonin production, high and low amplitudes of core temperatures) will be observed during 2 systematically permuted experimental shiftwork periods which are separated by 4 weeks. These studies are at present roughly planned. An adjustment of the design, the procedure, and the methods might be necessary due to the results of Steps 1 and 2, as well as to the then available knowledge provided by the studies of other authors. In principle, two or three days of dayshift will be followed by 5 days of nightwork. During one experiment, adaptation to night work will be facilitated by bright light that is individually applied according to the results of the constant routine in such a way that it causes a phase delay.

Physiological, psychological, and biochemical parameters that are likely to be influenced by the alterations of the circadian rhythm will be recorded as well as the respective effects on the ultradian rhythmicity, particularly on sleep. During the entire observation period core temperatures, heart rates and body movements will be recorded continuously throughout, the excretion of 6-hydroxymelatonin sulfate for every 3-hours period, and the electrophysiological indicators of sleep depth during the night. As melatonin is much less sensitive to masking than rectal temperature, the actual concentration of plasma melatonin will be determined hourly during the 24 hours of the last dayshift and the 24 hour period of the 3rd nightshift. During the time awake several tests concerning mental performance, such as implicite learning which proved to be sensitive against sleep disorders will be performed.

Step 4 – Hypothesis: Individual features (self-rated circadian phase / course and amplitude of body core temperature or of melatonin production) are reliable predictors for the ability to adapt to shiftwork.

The **prospective study** aims at the clarification, whether and to what extent the amount and the course of individual melatonin production correlates with the adaptability to shiftwork. Those persons who were investigated in the 2nd part of the study shall be asked to participate again after they had finished their education and worked in their profession for at least one year. First these persons complete again the questionnaire on subjective circadian phase and another questionnaire where they state their experience with shiftwork. As it cannot be expected that persons who had only recently finished their professional education and started their job frankly admit if they have serious problems with shiftwork, objective physiological measures are advisable. Body core temperatures and heart rates will be measured continuously and the excretion of 6-hydroxymelatonin sulfate for every 3-hours period. Actual concentration of plasma melatonin will be determined hourly during the 24 hour period of the last dayshift and the 24 hour period of the 3rd nightshift. These respective 2 nights shall be spent in the laboratory.

As the ability to adapt to shiftwork is supposed to be related to the individual circadian phase and persons with extreme phases (morning-, evening types) respectively persons with extremely low or high melatonin production are relatively seldom in the total population, it is necessary to arrange night shifts particularly for those persons (dependent on the results of part 2).

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